

09/905,188

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(FILE 'HOME' ENTERED AT 00:36:25 ON 25 JAN 2003)

FILE 'REGISTRY' ENTERED AT 00:36:34 ON 25 JAN 2003

L1           STRUCTURE UPLOADED  
L2         13 S L1 SSS SAM  
L3         6027 S L1 SSS FULL

FILE 'STNGUIDE' ENTERED AT 00:37:52 ON 25 JAN 2003

FILE 'REGISTRY' ENTERED AT 00:42:19 ON 25 JAN 2003

L4           STRUCTURE UPLOADED  
L5         11 S L4 SSS SAM  
L6         5427 S L5 SSS FULL

FILE 'CAPPLUS' ENTERED AT 00:43:10 ON 25 JAN 2003

L7         3 S L6 AND VASCULAR? AND (HYPER(2A)TENS? OR HYPERTENSION OR SYSTO  
L8         5 S L6 AND (HYPER(2A)TENS? OR HYPERTENSION OR SYSTOL?)

FILE 'STNGUIDE' ENTERED AT 00:46:13 ON 25 JAN 2003

FILE 'REGISTRY' ENTERED AT 00:58:41 ON 25 JAN 2003

L9           STRUCTURE UPLOADED  
L10        4 S L9 SSS SAM  
L11       1422 S L9 SSS FULL

FILE 'CAPPLUS' ENTERED AT 01:02:02 ON 25 JAN 2003

L12       2 S L11 AND (HYPER(2A)TENS? OR HYPERTENSION OR SYSTOL?)

Delacroix

09/905,188

(FILE 'HOME' ENTERED AT 00:36:25 ON 25 JAN 2003)

FILE 'REGISTRY' ENTERED AT 00:36:34 ON 25 JAN 2003

L1           STRUCTURE UPLOADED  
L2           13 S L1 SSS SAM  
L3           6027 S L1 SSS FULL

FILE 'STNGUIDE' ENTERED AT 00:37:52 ON 25 JAN 2003

FILE 'REGISTRY' ENTERED AT 00:42:19 ON 25 JAN 2003

L4           STRUCTURE UPLOADED  
L5           11 S L4 SSS SAM  
L6           5427 S L5 SSS FULL

FILE 'CAPLUS' ENTERED AT 00:43:10 ON 25 JAN 2003

L7           3 S L6 AND VASCULAR? AND (HYPER(2A)TENS? OR HYPERTENSION OR SYSTO  
L8           5 S L6 AND (HYPER(2A)TENS? OR HYPERTENSION OR SYSTOL?)

FILE 'STNGUIDE' ENTERED AT 00:46:13 ON 25 JAN 2003

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Delacroix

09/905,188

=> s 16 and vascular? and (hyper(2a)tens? or hypertension or systol?)  
1850 L6  
111752 VASCULAR?  
11661 HYPER  
386823 TENS?  
69 HYPER(2A)TENS?  
59195 HYPERTENSION  
17583 SYSTOL?  
L7 3 L6 AND VASCULAR? AND (HYPER(2A)TENS? OR HYPERTENSION OR SYSTOL?)

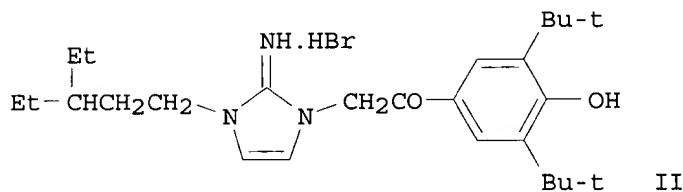
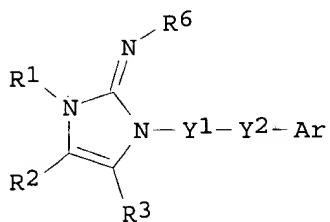
=> s 16 and (hyper(2a)tens? or hypertension or systol?)

1850 L6  
11661 HYPER  
386823 TENS?  
69 HYPER(2A)TENS?  
59195 HYPERTENSION  
17583 SYSTOL?

L8 5 L6 AND (HYPER(2A)TENS? OR HYPERTENSION OR SYSTOL?)

=> d 18 abs ibib kwic hitstr 1-5

L8 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS  
GI



AB The 2-iminoimidazole derivs. represented by the formula (I) or salts thereof [wherein R1, R2, R3 = H, cyano, halo, each (un)substituted C1-6 alkyl, alkylidene, C2-6 alkenyl, C2-6 alkynyl, acyl, CO2H, CONH2, C1-6 alkoxy carbonyl, C1-6 alkylaminocarbonyl, HO, C1-6 alkoxy, etc.; or R1 and R2 are linked together to form a 5-membered ring; R6 = H, C1-6 alkyl, acyl, CONH2, HO, C1-6 alkoxy, C1-6 alkyloxy carbonyloxy, C3-8 cycloalkyl, optionally acyloxy-substituted C1-6 alkyloxy carbonyl, etc.; Y1 = a single bond, (CH2)m (wherein m = an integer of 1-3), each (un)substituted CH, CH2, NH, CONH, or SO2NH, etc.; Y2 = a single bond, O, (CH2)m (m = same as above), CO, SO, SO2, each (un)substituted CH, CH2, or C(:NOH); Ar = H,

(un)substituted Ph or a 5- to 14-membered arom. heterocycl] are prep'd. These compds. are antagonists of thrombin receptors, in particular thrombin PAR1 receptor, platelet aggregation inhibitors, or proliferation inhibitors of smooth muscle cell, endothelial cell, fibroblast, kidney cell, osteosarcoma cell, muscle cell, cancer cell and/or glial cell. They are remedies and/or preventives of thrombosis, vascular restenosis, deep venous thrombosis, lung embolism, cerebral infarction, heart disease, disseminated intravascular coagulation syndrome, **hypertension**, inflammation, rheumatism, asthma, glomerulonephritis, osteoporosis, neuropathy and/or malignant tumor. Thus, a soln. of 305 mg 1-(3-ethylpentyl)-1H-2-imidazoleamine and 660 mg 2-bromo-1-[3,5-di(tert-butyl)-4-hydroxyphenyl]-1-ethanone in 20 mL ethanol was heated at 60.degree. for 3 h to give 700 mg 1-[3,5-di(tert-butyl)-4-hydroxyphenyl]-2-[3-(3-ethylpentyl)-2-imino-2,3-dihydroimidazol-1-yl]ethanone hydrobromide (II). II showed IC<sub>50</sub> of 0.074 .mu.M for inhibiting the [<sup>3</sup>H]Ala-(4-fluoro)Phe-Arg-(cyclohexyl)Ala-(homo)Arg-NH<sub>2</sub> binding on human platelet membrane in a thrombin receptor binding assay, that of 0.54 .mu.M for inhibiting the thrombin-induced human platelet aggregation, and that of 0.3 .mu.M for inhibiting the proliferation of rat aortic smooth muscle cell.

ACCESSION NUMBER: 2002:849599 CAPLUS  
 DOCUMENT NUMBER: 137:353022  
 TITLE: Preparation of 2-iminoimidazole derivatives as thrombin receptor antagonists  
 INVENTOR(S): Suzuki, Shuichi; Kotake, Makoto; Miyamoto, Mitsuaki; Kawahara, Tetsuya; Kajiwara, Akiharu; Hishinuma, Ieharu; Okano, Kazuo; Miyazawa, Syuhei; Clark, Richard; Ozaki, Fumihiro; Sato, Nobuaki; Shinoda, Masanobu; Kamada, Atsushi; Tsukada, Itaru; Matsuura, Fumiyo; Naoe, Yoshimitsu; Terauchi, Taro; Oohashi, Yoshiaki; Ito, Osamu; Tanaka, Hiroshi; Musya, Takashi; Kogushi, Motoji; Kawada, Tsutomu; Matsuoka, Toshiyuki; Kobayashi, Hiroko; Chiba, Kenichi; Kimura, Akifumi; Ono, Naoto  
 PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 171 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 4  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088092	A1	20021107	WO 2002-JP3950	20020419
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.:		JP 2001-121829	A	20010419
		JP 2001-269422	A	20010905
OTHER SOURCE(S):	MARPAT	137:353022		

AB . . . remedies and/or preventives of thrombosis, vascular restenosis, deep venous thrombosis, lung embolism, cerebral infarction, heart disease, disseminated intravascular coagulation syndrome, **hypertension**, inflammation, rheumatism, asthma, glomerulonephritis, osteoporosis, neuropathy and/or malignant tumor. Thus, a soln. of 305 mg 1-(3-ethylpentyl)-1H-2-imidazoleamine and 660 mg 2-bromo-1-[3,5-di(tert-butyl)-4-hydroxyphenyl]-1-ethanone.

ST . . . cerebral infarction prevention treatment iminoimidazole prepn; heart disease prevention treatment iminoimidazole prepn; disseminated intravascular coagulation syndrome prevention treatment iminoimidazole prepn; **hypertension** prevention treatment iminoimidazole prepn; inflammation prevention treatment iminoimidazole prepn; rheumatism prevention treatment iminoimidazole prepn; asthma prevention treatment iminoimidazole prepn; glomerulonephritis. . .

IT Anti-inflammatory agents  
 Antiasthmatics  
 Anticoagulants  
 Antihypertensives  
 Antirheumatic agents  
 Antitumor agents  
 Asthma  
 Cardiovascular agents  
 Cytotoxic agents  
 Heart, disease  
 Human  
**Hypertension**  
 Inflammation  
 Osteoporosis  
 Platelet aggregation inhibitors  
 Rheumatic diseases  
 Thrombosis  
 (prepn. of 2-iminoimidazole derivs. as thrombin receptor antagonists, platelet aggregation inhibitors, or cell proliferation inhibitors for prevention and/or treatment of diseases)

IT	473936-54-8P	474671-16-4P	474671-18-6P	474671-19-7P	474671-20-0P
	474671-21-1P	474671-22-2P	474671-23-3P	474671-25-5P	474671-26-6P
	474671-27-7P	474671-28-8P	474671-30-2P	474671-31-3P	474671-32-4P
	474671-33-5P	474671-34-6P	474671-36-8P	474671-37-9P	474671-38-0P
	474671-39-1P	474671-40-4P	474671-41-5P	474671-42-6P	474671-44-8P
	474671-46-0P	474671-48-2P	474671-49-3P	474671-50-6P	474671-51-7P
	474671-52-8P	474671-53-9P	474671-54-0P	474671-55-1P	474671-56-2P
	474671-57-3P	474671-58-4P	474671-59-5P	474671-60-8P	474671-61-9P
	474671-62-0P	474671-63-1P	474671-64-2P	474671-65-3P	474671-66-4P
	474671-67-5P	474671-68-6P	474671-69-7P	474671-70-0P	474671-71-1P
	474671-73-3P	474671-74-4P	474671-75-5P	474671-76-6P	474671-77-7P
	474671-78-8P	474671-79-9P	474671-80-2P	474671-81-3P	474671-82-4P
	474671-83-5P	474671-84-6P	474671-85-7P	474671-86-8P	474671-87-9P
	474671-88-0P	474671-89-1P	474671-90-4P	474671-91-5P	474671-92-6P
	474671-93-7P	474671-94-8P	474671-95-9P	474671-96-0P	474671-97-1P
	474671-98-2P	474671-99-3P	474672-00-9P	474672-01-0P	474672-02-1P
	474672-03-2P	474672-04-3P	474672-05-4P	474672-06-5P	474672-07-6P
	474672-08-7P	474672-09-8P	474672-10-1P	474672-11-2P	474672-14-5P
	474672-15-6P	474672-18-9P	474672-21-4P	474672-23-6P	474672-25-8P
	474672-27-0P	474672-28-1P	474672-29-2P	474672-30-5P	474672-31-6P
	474672-32-7P	474672-33-8P	474672-34-9P	474672-35-0P	474672-36-1P
	474672-37-2P	474672-38-3P	474672-39-4P	474672-40-7P	474672-41-8P
	474672-42-9P	474672-44-1P	474672-45-2P	474672-46-3P	
	<b>474672-47-4P</b>	<b>474672-48-5P</b>	<b>474672-49-6P</b>	<b>474672-50-9P</b>	

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474672-51-0P 474672-52-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 2-iminoimidazole derivs. as thrombin receptor antagonists, platelet aggregation inhibitors, or cell proliferation inhibitors for prevention and/or treatment of diseases)

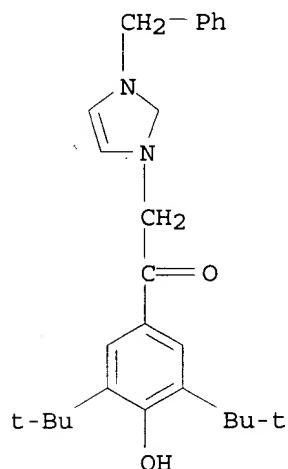
IT 474672-47-4P 474672-48-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 2-iminoimidazole derivs. as thrombin receptor antagonists, platelet aggregation inhibitors, or cell proliferation inhibitors for prevention and/or treatment of diseases)

RN 474672-47-4 CAPLUS

CN 1H-Imidazolium, 1-[2-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-2-oxoethyl]-3-(phenylmethyl)-, bromide (9CI) (CA INDEX NAME)



● Br<sup>-</sup>

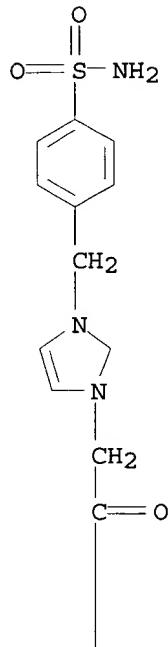
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RN 474672-48-5 CAPLUS

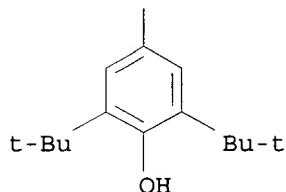
CN 1H-Imidazolium, 1-[4-(aminosulfonyl)phenylmethyl]-3-[2-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-2-oxoethyl]-, bromide (9CI) (CA INDEX NAME)

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PAGE 1-A



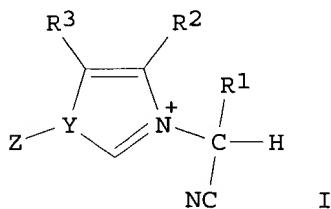
PAGE 2-A



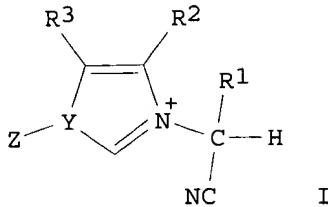
\*\*\* FRAGMENT DIAGRAM IS INCOMPLETE \*\*\*

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS  
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AB The prepn. cyanomethyl substituted thiazoliums and imidazoliums [I; wherein Y = N, S; Z is absent if Y is S, and, if present = (C1-C7)alkyl, vinyl, allyl, arylcarbonyl, amino, etc.; R1, R4, independently = H, alkyl, Ph optionally substituted with one or more halogen, alkyl, di(lower alkyl)amino, or alkoxy groups; R2, R3 = H, acylamino, acyloxyalkyl, alkanoyl, etc.] is described. Thus, 1-methylimidazole and bromoacetonitrile were reacted to give 1-methyl-3-(2-cyanomethylene)-imidazolium bromide. The prepd. compds. are useful in improving the elasticity or reducing wrinkles of a skin, treating diabetes or treating/inhibiting/ameliorating discoloration of teeth, adverse sequelae of diabetes, kidney damage, damage to blood vasculature, hypertension, retinopathy, damage to lens proteins, cataracts, peripheral neuropathy, osteoarthritis, damage to cardiovascular tissue due to heart failure, or improving myocardial elasticity, or preventing damage to tissues in the i.p. cavity caused by contact with elevated levels of reducing sugars.

ACCESSION NUMBER: 2002:90030 CAPLUS  
 DOCUMENT NUMBER: 136:134758  
 TITLE: Preparation of cyanomethyl substituted thiazoliums and imidazoliums and treatments of disorders associated with protein aging  
 INVENTOR(S): Wagle, Dilip; Fang, Sheng Ding  
 PATENT ASSIGNEE(S): Alteon, Inc., USA  
 SOURCE: PCT Int. Appl., 52 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008210	A1	20020131	WO 2001-US22200	20010713
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002068729	A1	20020606	US 2001-905188	20010713
US 2002103182	A1	20020801	US 2001-905035	20010713
US 2002177586	A1	20021128	US 2001-37447	20011231
PRIORITY APPLN. INFO.:			US 2000-218273P	P 20000713
			US 2000-259431P	P 20001229
			US 2001-259242P	P 20010102

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US 2001-296435P P 20010606  
US 2001-905188 A1 20010713

OTHER SOURCE(S): MARPAT 136:134758

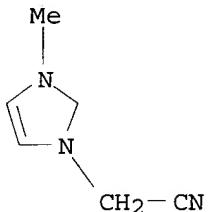
AB . . . of a skin, treating diabetes or treating/inhibiting/ameliorating discoloration of teeth, adverse sequelae of diabetes, kidney damage, damage to blood vasculature, **hypertension**, retinopathy, damage to lens proteins, cataracts, peripheral neuropathy, osteoarthritis, damage to cardiovascular tissue due to heart failure, or improving myocardial.

IT 392710-36-0P 392710-37-1P 392710-38-2P 392710-39-3P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of cyanomethyl substituted thiazoliums and imidazoliums and treatments of disorders assocd. with protein aging)

IT 392710-36-0P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of cyanomethyl substituted thiazoliums and imidazoliums and treatments of disorders assocd. with protein aging)

RN 392710-36-0 CAPLUS

CN 1H-Imidazolium, 1-(cyanomethyl)-3-methyl-, bromide (9CI) (CA INDEX NAME)

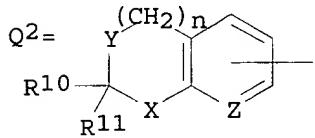
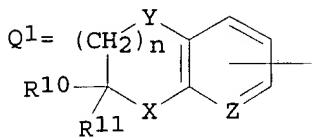
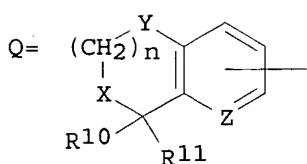
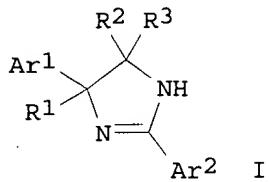


④ Br<sup>-</sup>

\*\*\* FRAGMENT DIAGRAM IS INCOMPLETE \*\*\*

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS  
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AB Compds. represented by the general formula (I) [wherein Ar1, Ar2, Ar3 = aryl or heteroaryl each optionally having substituents selected from cyano, halo, NO<sub>2</sub>, lower alkyl, halo-lower alkyl, hydroxy-lower alkyl, lower cycloalkyl-lower alkyl, lower alkenyl, lower alkylamino, di-lower alkylamino, lower alkanoylamino, lower alkylsulfonylamino, arylsulfonylamino, HO, lower alkoxy, halo-lower alkoxy, aryloxy, heteroaryloxy, lower alkylthio, CO<sub>2</sub>H, CHO, lower alkanoyl, lower alkoxy carbonyl, CONH<sub>2</sub>, lower alkylcarbamoyl, di-lower alkylcarbamoyl, lower alkylsulfonyl, arylsulfonyl, aryl, and heteroaryl; n = 0,1; R1 = lower cycloalkyl, Ar3, Q, Q1, Q2; R1, R2 = H, lower cycloalkyl, lower alkenyl, lower alkyl optionally having substituents selected from halo, lower alkylamino, di-lower alkylamino, lower alkanoylamino, HO, lower alkoxy, CHO, lower alkoxy carbonyl, lower alkylcarbamoyl, and di-lower alkylcarbamoyl; wherein R10 = R11 = H, or R10 and R11 together represents oxo; X, Y = CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>, NR<sub>12</sub> (wherein R<sub>12</sub> = H, lower alkyl), O, S; Z = CH, N; with the proviso that when R2 and R3 are simultaneously hydrogen, Ar1, Ar2 and R1 do not simultaneously represent unsubstituted phenyl or salts or esters thereof are prepd. Theses compds. are useful as therapeutic agents for treating various neuropeptide Y (NPY)-related diseases, for example, circulatory diseases including hypertension, kidney diseases, cardiac diseases, vasospasm, and arteriosclerosis; central nervous system diseases including hyperphagia, depression, anxiety, convulsion, epilepsy, dementia, pain, alc. dependence, and withdrawal symptoms due to abstinence from drugs; metabolic diseases including obesity, diabetes, hormonal disorders, hypercholesterolemia, and hyperlipidemia; sexual dysfunction and reproductive function disorders; digestive diseases including enterokinetic disorders; respiratory diseases; inflammation; or glaucoma. Thus, 46.5 mg 2,4-dicyanopyridine and 24 mg ytterbium trifluoromethanesulfonate were added to a soln. of 100 mg (2S)-1-(4-fluorophenyl)-1-(6-fluoro-3-pyridyl)-1,2-propanediamine in 0.25 mL PhMe and stirred at 100.degree. for 5 h to give 106 mg optically active (5S)-2-(4-cyano-2-pyridyl)-4-(4-fluorophenyl)-4-(6-fluoro-3-pyridyl)-5-methyl-2-imidazolidine (II). II in vitro showed IC<sub>50</sub> of 1.7 nM for inhibiting the binding of [<sup>125</sup>I]peptide YY to human NPY receptor. Tablet formulations contg. 2-(3-cyanophenyl)-4,4-bis(4-fluorophenyl)-2-imidazolidine were prepd.

ACCESSION NUMBER: 2001:636055 CAPLUS  
 DOCUMENT NUMBER: 135:211050  
 TITLE: Preparation of imidazoline compounds as antagonists of neuropeptide Y receptor  
 INVENTOR(S): Sato, Nagaaki; Okamoto, Osamu; Jitsuoka, Makoto;

Nagai, Keita; Kanatani, Akio; Ishihara, Akane; Ishii,  
 Yasuyuki; Fukami, Takehiro  
 PATENT ASSIGNEE(S) : Banyu Pharmaceutical Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 137 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062738	A1	20010830	WO 2001-JP1312	20010222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001034128	A5	20010903	AU 2001-34128	20010222
EP 1264826	A1	20021211	EP 2001-906215	20010222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			JP 2000-45042	A 20000222
			WO 2001-JP1312	W 20010222

OTHER SOURCE(S) : MARPAT 135:211050

AB . . . prepd. Theses compds. are useful as therapeutic agents for treating various neuropeptide Y (NPY)-related diseases, for example, circulatory diseases including hypertension, kidney diseases, cardiac diseases, vasospasm, and arteriosclerosis; central nervous system diseases including hyperphagia, depression, anxiety, convulsion, epilepsy, dementia, pain, alc.. . .

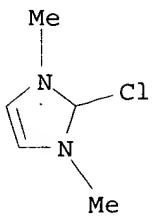
IT 93-60-7, Nicotinic acid methyl ester 98-97-5, Pyrazinecarboxylic acid 345-92-6, 4,4'-Difluorobenzophenone 352-13-6, 4-Fluorophenylmagnesium bromide 766-11-0, 5-Bromo-2-fluoropyridine 1493-23-8, 4-Fluorophenyllithium 1877-72-1, 3-Cyanobenzoic acid 7471-86-5, Benzimidic acid methyl ester 7677-24-9, Trimethylsilyl cyanide 13368-86-0, 1,2,5-Thiadiazole-3-carboxylic acid 29181-50-8, 2,4-Dicyanopyridine 56133-37-0, 4-Iothiazolecarboxylic acid methyl ester 60573-68-4, 3-Pyridyllithium 74617-55-3 95407-05-9 97316-50-2 **125376-11-6**, 2-Chloro-1,3-dimethylimidazolium chloride 146374-27-8 357925-36-1 357925-37-2 357925-43-0 357926-58-0 357926-67-1 357926-97-7 357927-02-7 357927-05-0 357927-08-3 357927-10-7 357927-11-8 357927-49-2 357927-50-5

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (prepn. of imidazoline compds. as antagonists of neuropeptide Y receptor)

IT **125376-11-6**, 2-Chloro-1,3-dimethylimidazolium chloride  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (prepn. of imidazoline compds. as antagonists of neuropeptide Y receptor)

RN 125376-11-6 CAPLUS  
 CN 1H-Imidazolium, 2-chloro-1,3-dimethyl-, chloride (9CI) (CA INDEX NAME)

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\*\*\* FRAGMENT DIAGRAM IS INCOMPLETE \*\*\*

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS

AB Described is a method for modulating the phenotype of a cell, and particularly, of a target cell in a patient who has or is at risk of developing a disease or condition in which is assocd. with dysregulation of cellular phenotype. The method includes administration of a recombinant nucleic acid mol. encoding a protein having cAMP responsive element-binding (CREB) biol. activity or dominant neg. CREB biol. activity to a patient, in such a manner that the protein is expressed in a target cell of a patient and is sufficient to modulate the phenotype of the target cell. CREB is necessary and sufficient to initiate adipocyte differentiation, based on its constitutive expression in 3T3-L1 fibroblasts prior to the induction of adipogenesis and throughout the differentiation process. Furthermore, both CREB phosphorylation and transcriptional activity are rapidly induced in 3T3-L1 fibroblasts by conventional differentiation-inducing agents, and CREB binds to and stimulates transcription from the promoters of several adipocyte-specific genes. Augmentation of CREB protein expression by adenovrial gene transfer at the time of angioplasty will promoter smooth muscle cell differentiation and thereby decrease post-angioplasty restenosis. Such a method is particularly useful in patients who have, or at risk of developing, diabetes, obesity, macrovascular disease, heart failure, osteoarthritis, and neural diseases and conditions.

ACCESSION NUMBER: 2001:300737 CAPLUS

DOCUMENT NUMBER: 134:321579

TITLE: Modulation of cell phenotype by transformation with cAMP responsive element-binding proteins

INVENTOR(S): Reusch, Jane E.; Klemm, Dwight J.

PATENT ASSIGNEE(S): University Technology Corporation, USA; National Jewish Medical and Research Center; U.S. Government as Represented by the Department of Veterans Affairs

SOURCE: PCT Int. Appl., 155 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001029062	A2	20010426	WO 2000-US28316	20001012

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WO 2001029062 A3 20010913  
WO 2001029062 C2 20020808  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,  
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001010829 A5 20010430 AU 2001-10829 20001012

PRIORITY APPLN. INFO.: US 1999-420060 A 19991018  
WO 2000-US28316 W 20001012

IT **Hypertension**

(pulmonary, CREB effect in vascular smooth muscle on; modulation of cell phenotype by transformation with cAMP responsive element-binding proteins)

IT 57-88-5, Cholesterol, biological studies 2390-68-3, DDAB 104162-48-3,  
Dotma 144189-73-1, DOTAP 169619-96-9, DOTIM

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(modulation of cell phenotype by transformation with cAMP responsive element-binding proteins)

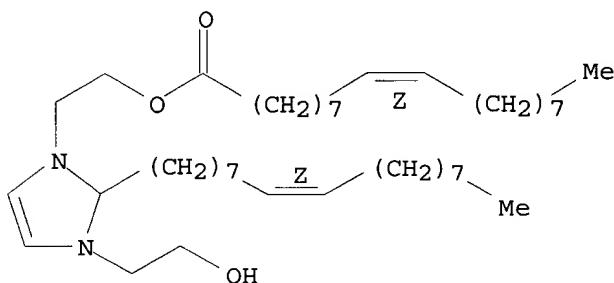
IT **169619-96-9**, DOTIM

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(modulation of cell phenotype by transformation with cAMP responsive element-binding proteins)

RN 169619-96-9 CAPLUS

CN 1H-Imidazolium, 2-[(8Z)-8-heptadecenyl]-1-(2-hydroxyethyl)-3-[2-[(9Z)-1-oxo-9-octadecenyl]oxy]ethyl]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



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L8 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS

AB The authors report gene transfer to the normal and injured murine pulmonary circulation via systemic (intravascular) and airway (intratracheal) delivery of novel polycationic liposomes (imidazolium chloride, imidazolinium chloride-cholesterol, and Et phosphocholine). With use of the reporter genes chloramphenicol acetyltransferase (CAT) or human placental alk. phosphatase (hpAP), intravascular injection of

lipid-DNA complexes resulted in gene expression primarily in the lung, with lesser expression in the heart (11% of lung) and spleen (8% of lung). Histochem. staining for the hpAP reporter gene showed localized transgene expression in the microvascular endothelium. Monocrotaline (80 mg/kg body wt s.c.) treatment produced endovascular inflammation and reduced lung CAT activity (2 days postintravascular transfection) by 75.+-.8 and 86.+-.6% at 7 and 21 days, resp., after monocrotaline. Despite the apparent decrease in functional CAT protein, Southern blot anal. suggested maintained plasmid delivery, whereas quant. PCR (TaqMan) showed decreased CAT mRNA levels in monocrotaline mice. In contrast, intratracheal delivery of lipid-DNA complexes showed enhanced CAT expression in monocrotaline mice. Transfection in alternate pulmonary vascular disorders was studied by inducing hypoxic pulmonary **hypertension** (4 wk at barometric pressure of 410 mmHg). Efficiency and duration of gene transfer, assessed by CAT activity, were similar in pulmonary hypertensive and normal lungs. The authors conclude that imidazolinium-derived polycationic liposomes provide a means of relatively selective and efficient gene transfer to the normal and injured murine microvascular circulation, although translation of transgene mRNA may be reduced by preexisting endothelial injury.

ACCESSION NUMBER: 2000:16851 CAPLUS  
 DOCUMENT NUMBER: 132:298747  
 TITLE: Vascular inflammation inhibits gene transfer to the pulmonary circulation in vivo  
 AUTHOR(S): Tyler, Robert C.; Fagan, Karen A.; Unfer, Robert C.; Gorman, Cornelia; McClarrion, Molly; Bullock, Clayton; Rodman, David M.  
 CORPORATE SOURCE: Cardiovascular Pulmonary Research Laboratory, University of Colorado Health Sciences Center, Denver, CO, 80262, USA  
 SOURCE: American Journal of Physiology (1999), 277(6, Pt. 1), L1199-L1204  
 CODEN: AJPHAP; ISSN: 0002-9513  
 PUBLISHER: American Physiological Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB . . . complexes showed enhanced CAT expression in monocrotaline mice. Transfection in alternate pulmonary vascular disorders was studied by inducing hypoxic pulmonary **hypertension** (4 wk at barometric pressure of 410 mmHg). Efficiency and duration of gene transfer, assessed by CAT activity, were similar. . .  
 IT Blood vessel, disease  
 Circulation  
**Hypertension**  
 (pulmonary; imidazolinium-derived polycationic liposomes for i.v. and intratracheal gene transfer to normal and injured murine pulmonary microvascular circulation is inhibited by pulmonary vascular inflammation)  
 IT 57-88-5, Cholesterol, biological studies 169619-96-9, DOTIM  
 183283-19-4, EDMPC 264196-93-2  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (imidazolinium-derived polycationic liposomes for i.v. and intratracheal gene transfer to normal and injured murine pulmonary microvascular circulation is inhibited by pulmonary vascular inflammation)  
 IT 169619-96-9, DOTIM

09/905,188

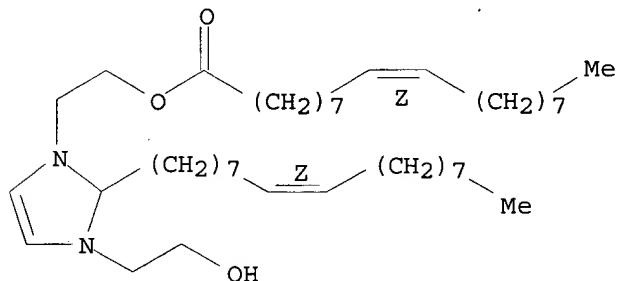
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(imidazolinium-derived polycationic liposomes for i.v. and intratracheal gene transfer to normal and injured murine pulmonary microvascular circulation is inhibited by pulmonary vascular inflammation)

RN 169619-96-9 CAPLUS

CN 1H-Imidazolium, 2-[<sup>8Z</sup>-(8Z)-8-heptadecenyl]-1-(2-hydroxyethyl)-3-[2-[[<sup>9Z</sup>-(9Z)-1-oxo-9-octadecenyl]oxy]ethyl]-, chloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● Cl<sup>-</sup>

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REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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